

Routine Laboratory Investigations in Infants and Children Presenting with Fever and Seizures at the University Hospital of the West Indies

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ABSTRACT

A retrospective chart review of the case notes of all children aged 6 months to 8 years presenting with fever and seizures to the University Hospital of the West Indies (UHWI) between January 2000 and December 2004 was conducted. Descriptive analyses were performed. Fifty-nine children (median age 1.58 years, range 0.58 to 6.83 years) were entered into the study. The main laboratory abnormalities were metabolic acidosis (23%), anaemia (10%), leukocytosis (35%) and hypomagnesaemia (3%). These were not significantly associated with meningitis or an underlying bacterial infection. There were no significant episodes of hyponatraemia, hypocalcaemia or hypoglycaemia. Meningitis was uncommon and occurred in only two (3.4%) children both younger than 16 months of age and who had other abnormal clinical signs. This study demonstrated that routine performance of haematological and biochemical investigations in children presenting with seizures and fever were of limited value. Lumbar punctures in children older than age 18 months with no other abnormal clinical signs were also found to be of low yield. Current American Academy of Paediatrics (AAP) recommendations that serum electrolytes, calcium, phosphate, magnesium, complete blood count and blood glucose should not be performed routinely in a child with a first simple febrile seizure can be safely applied to this study population.

Investigaciones de Rutina en el Laboratorio en Relación con Infantes y Niños que se Presentan con Fiebre y Convulsiones en el Hospital Universitario de West Indies

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RESUMEN

Se llevó a cabo un estudio retrospectivo de las historias clínicas en busca de notas sobre los casos de todos los niños de 6 meses a 8 años de edad que se presentaron con fiebre y convulsiones en el Hospital Universitario de West Indies (HUWI) entre enero de 2000 y diciembre de 2004. Se realizaron análisis descriptivos. Cincuenta y nueve niños (edad mediana (1.58 años, rango 0.58 a 6.83 años) formaron parte de este estudio. Las principales anomalías halladas mediante el laboratorio fueron: acidosis metabólica (23%), anemia (10%), leucocitosis (35%), e hipomagnesemia (3%). Éstas no estuvieron significativamente asociadas con meningitis o alguna infección bacteriana subyacente. No hubo episodios significativos de hiponatremia, hipocalcemia o hipoglicemia. La meningitis fue poco común, ocurriendo sólo en dos niños (3.4%), ambos con menos de 16 meses de edad y con otros signos clínicos anormales. Este estudio demostró que el trabajo de rutina realizado en las investigaciones hematológicas y bioquímicas en los niños que se presentaron con fiebre y convulsiones, tuvo un valor limitado. También se halló que las punciones lumbares realizadas a niños de más de 18 meses sin ningún otro signo clínico anormal, tuvieron poco valor. Las recomendaciones actuales de la Academia Americana de Pediatría (AAP) en cuanto a que las pruebas de electrolitos en suero, las mediciones de calcio, fosfato, magnesio, el conteo sanguíneo completo, y la prueba de glucosa en sangre, no deben ser realizadas rutinariamente en un niño con una primera simple convulsión febril, pueden ser aplicadas con seguridad a esta población bajo estudio.

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INTRODUCTION

A febrile seizure (FS) is defined as a seizure event in infancy or childhood, usually occurring between three months and five years of age, associated with fever but without evidence of intracranial infection or other definable cause. Febrile seizures are the commonest seizure types in children. The fever associated with febrile convulsions is most often caused by upper respiratory tract infections, gastroenteritis and urinary tract infections (1, 2). Occult bacteraemia occurs in approximately 2% of cases of febrile seizures (3); this is no more frequent than with fever alone. The prevalence of meningitis in children with seizures and fever in North American paediatric emergency wards is between 0% and 2% (4).

Specific guidelines for the investigation of children with first simple, febrile seizures were published by the American Academy of Paediatrics (AAP) in 1996 (5). This recommendation states that after the first seizure with fever in infants younger than 12 months, performance of a lumbar puncture should be strongly considered because the clinical signs and symptoms associated with meningitis may be minimal or absent in this age group. In a child between 12 and 18 months of age, a lumbar puncture should be considered because clinical signs and symptoms of meningitis may be subtle. In a child older than 18 months, although a lumbar puncture is not routinely warranted, it is recommended in the presence of meningeal signs and symptoms (*ie* neck stiffness, Kernigs and Brudzinski signs) or for any child whose history or examination results suggest the presence of intracranial infection. In infants and children who have had febrile seizures and have received prior antibiotic treatment, clinicians should be aware that treatment can mask the signs and symptoms of meningitis. A lumbar puncture should be strongly considered. The AAP recommends that the following determinations should not be performed routinely in the evaluation of a child with a first simple febrile seizure: serum electrolytes, calcium, phosphorus, magnesium, complete blood count or blood glucose.

There is no national consensus or policy on routine lumbar punctures and laboratory evaluations in infants and children presenting with seizures during a febrile illness. A study was therefore conducted to investigate the value of haematological, biochemical and cerebrospinal fluid evaluations in children presenting with fever and seizures to the University Hospital of the West Indies (UHWI).

SUBJECTS AND METHODS

The records of all children ages 6 months to 8 years presenting with fever and seizures or diagnosed with febrile seizures or meningitis between January 2000 and December 2004 at the paediatric medical wards, accident and emergency and casualty departments of the UHWI were reviewed. These cases were identified by reviewing the admission registers and study cases fulfilling the case definition were selected. Data were collected from medical records and re-

corded on a data extraction sheet which provided demographic information, details of the perinatal history, past medical history, family history as well as the details of the current illness, the investigations, treatment and outcome.

Clinical Definition

A febrile seizure is an acute seizure event associated with a temperature $\geq 38^{\circ}\text{C}$ but without evidence of underlying neurological disorder or other definable cause. Children with a history of previous unprovoked afebrile seizures or with known neurological illness were excluded.

Complex febrile seizure – a seizure occurring in the presence of a temperature $\geq 38^{\circ}\text{C}$ associated with one or more of the following; duration greater than 15 minutes, partial or focal seizures or greater than one seizure episode during one febrile illness.

Abnormal cerebrospinal fluid (CSF) results were defined as the presence of one or more of the following: greater than 5 wbc/mm³ of CSF, CSF/blood glucose ratio less than 0.5, CSF protein greater than 400 mg/dL, positive gram stain and culture. Descriptive analyses were performed using chi-square or Fisher's exact test. Statistical significance was taken at the level of $p < 0.05$. Ethical approval was granted by the Ethics Committee of the Faculty of Medical Sciences, The University of the West Indies/University Hospital of the West Indies.

RESULTS

Sixty of sixty-four (94%) files of patients were available for review. There was no difference in age or gender distribution between the four children whose case notes were unavailable and the study population.

There were forty-five (75%) males. The median age was 1.58 years (range 0.58 to 6.83 years). Fifty-nine (98%) were presenting with their first seizure episode and 1 (2%) with a recurrent episode. Fifty-five (92%) children presented with generalized seizures. The most frequent subtype in 31 (51.7%) children was generalized tonic clonic seizures. The seizure duration ranged from 0.25 minutes to 60 minutes with a median of 5 minutes. The majority of patients (45, 75%) had seizures lasting less than or equal to 15 minutes; 5 (8%) patients had seizures lasting greater than 30 minutes (*status epilepticus*).

Twenty-seven (45%) patients had complex febrile seizures on presentation. There was no significant association of complex febrile seizures with age of presentation, meningitis, CSF abnormality or positive bacterial culture.

The main laboratory abnormalities present were metabolic acidosis in 14 (23%), anaemia in 6 (10%), leukocytosis in 21 (35%) and hypomagnesaemia in 2 (3%) children. There were no episodes of hyponatraemia, hypocalcaemia or hypoglycaemia.

Thirty-six (72%) children had serum bicarbonate analysis performed. Fourteen (39%) children had metabolic acidosis defined as serum bicarbonate less than 15 mmol/L.

Their ages ranged from 0.83 – 4.16 years with a mean of 1.70 \pm 1.06 years. Metabolic acidosis was not associated with the presence of complex febrile seizures, diarrhoeal illness, meningitis or sepsis.

Haemoglobin estimation was performed for 59 (98%) children. Six (10%) children were anaemic (Hb < 10g/dL). These children's ages ranged from 1.0 – 2.0 years with a mean of 1.48 \pm 0.36 years. There was no significant association of anaemia with gender, the presence of an infection or meningitis.

Fifty-nine (98%) children had estimation of peripheral white blood cell count; 21(35%) children had leukocytosis (WBC > 15 x 10³/mm³). Leukocytosis was not significantly associated with the presence of an infection or with complex febrile seizures (Table 1).

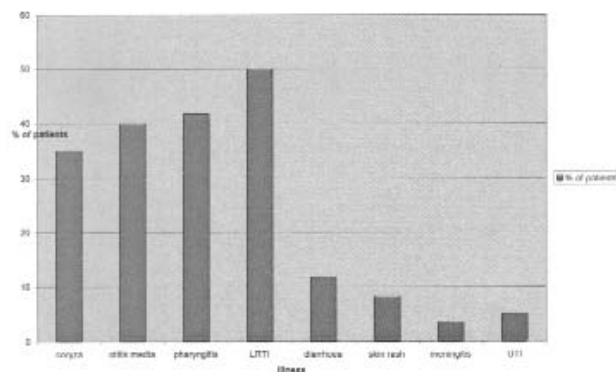
Table 1: Factors associated with the presence of leukocytosis in children with fever and seizures at the UHWI

Variable	Leukocytosis Present (%) n = 21	Leukocytosis Absent (%) n = 38	P value (chi-square or Fisher's exact test)
Gender			
Male	19 (91)	25 (66)	0.034
Female	2 (9)	13 (34)	
Complex seizures			
Yes	6 (32)	21(58)	0.054
No	13 (68)	15(42)	
Meningitis			
Positive	1 (5)	1 (3)	0.589
Negative	20 (95)	37 (97)	
Sepsis			
Positive	1 (5)	1 (5)	0.721
Negative	19 (95)	35 (95)	
UTI			
Positive	2 (13)	1 (4)	0.286
Negative	13 (87)	24 (96)	
Any bacterial cultures			
Positive	3 (14)	3 (8)	0.361
Negative	18 (86)	35 (92)	

Seventeen children (28%) had analysis of serum magnesium; 2 (3%) children were found to have hypomagnesaemia (Mg < 0.65 mmol/L). Both were males ages 0.58 and 1.25 years respectively; one patient presented with partial seizures and the other with hypotonic seizures.

Most children had an underlying respiratory illness (Fig. 1). Six (10%) children had positive bacterial cultures. Three children had urinary tract infections (*E coli* was isolated in one child and Coagulase negative staphylococcus in 2 children). One child had *H influenza* sepsis and meningitis and two blood specimen cultures grew Coagulase negative staphylococcus (Table 2).

Fifty-two (86.7%) children had complete CSF analysis – cytology, chemistry and microbiology. Eleven (21.2%)



Of note, a patient could have more than one associated illness at presentation.

Fig. 1: Associated illnesses in children presenting with fever and seizures at the UHWI.

Table 2: Positive microbial cultures isolated in children presenting with fever and seizures to the UHWI

Test	No of patients tested (%)	No. of positive tests (%)	Organisms
CSF culture	52 (87)	1 (2)	Haemophilus Influenza
Blood culture	58 (97)	3 (5)	1 Haemophilus influenza 2 Coag Neg Staph
Urine culture	41 (68)	3 (7)	1 Group D Strep 1 Coag Neg Staph 1 E Coli
Throat swab (bacterial)	15 (25)	1 (7)	Enterobacter
Stool OCP/ Culture	7 (12)	1 (14)	Ascaris
Rectal swab (viral)	7 (12)	0 (0)	–
Throat swab (viral)	10 (16)	0 (0)	–
Viral titres	6 (10)	1 (16)	Adenovirus

children had abnormal CSF findings. Two (one male and one female) were diagnosed with meningitis (one culture positive). Both were younger than 16 months of age. One child presented with generalized tonic-clonic seizures and the other with a hypotonic episode. Both seizures were simple febrile seizures; the temperature on presentation was 38.4 and 38.5°C respectively. Both presented with impaired consciousness without focal deficit. One child had meningism on clinical examination; this child had a positive CSF culture. The child with culture negative meningitis did not have a history of prior antibiotic use.

DISCUSSION

In this patient population, there was a high rate of laboratory investigations with 72% having blood urea, creatinine and electrolyte estimations, and 92–98% having complete blood counts, blood cultures and lumbar punctures for CSF analysis.

A recent US multicentre study of the patterns of the emergency department (ED) evaluation of febrile seizures with respect to the 1996 AAP guidelines found an overall lumbar puncture rate of 5.2%, consistent with adherence to the guidelines (6). One other study undertaken to describe the use of lumbar punctures in children younger than age 18 months found a rate of lumbar punctures of 24% in the 13–18-month age group and 28% in those 12 months and younger and that there were no adverse outcomes in those not receiving a lumbar puncture (7). In the patient population studied, only two children had meningitis; both were younger than age 18 months and presented with signs that would have indicated the need for a lumbar puncture – impaired consciousness and meningism. Routine lumbar punctures in children older than age 18 months with febrile seizures are therefore not likely to have significant yield.

Anaemia was found in 10% of patients and there was no significant association with meningitis or significant illness. The prevalence of anaemia in Jamaican children of this age is not known. However in an older population of rural Jamaican children, age 9 to 13 years, anaemia occurred in 14.7% (8). The prevalence of anaemia found in this study population may therefore be reflective of the overall prevalence rate for Jamaican children of that age group.

Although routine biochemical evaluations yielded metabolic acidosis in 23%, this finding was not significantly associated with sepsis, meningitis or even complex febrile seizures. One would therefore be unable to predict which child was likely to be acidotic based on clinical presentation and this finding, even if present, does not seem to suggest an increased likelihood of sepsis or other infectious syndrome. No child had hypoglycaemia, hyponatraemia or hypocalcaemia.

There was a low yield of positive bacterial cultures 2%, 5% and 7% for CSF, blood and urine respectively. This is comparable with international data which demonstrate a rate of meningitis 0–5%, occult bacteraemia 1–5% and urinary tract infection 1–5% in children presenting with fever and seizures (4, 9, 10, 11). These rates are comparable to that found in children presenting with a febrile illness in general, and therefore, the mere presence of seizures in a febrile child does not appear to increase the likelihood of bacterial infection.

The findings of this study are therefore congruent with the 1996 recommendation of the American Academy of Pediatrics. The routine performance of laboratory investigations in children presenting with fever and seizures is of low yield. The performance of lumbar punctures and bacterial cultures in children with fever and seizures should be individualized and based on the clinical presentation. Considering the financial burden and physical discomfort experienced by the child and family, and the cost in terms of time, manpower and resources of biochemical and haematological evaluations in children presenting with fever and seizure which are of low yield, the 1996 AAP recommendations that serum electrolytes, calcium, phosphate, magnesium, complete blood count and blood glucose be not performed routinely in a child with a first simple febrile seizure can therefore be safely applied to this study population.

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